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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/649,944	08/28/2003	Ralph M. Ellison	077319-0384	7142

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EXAMINER	
PAK, JOHN D	
ART UNIT	**PAPER NUMBER**
1616	

DATE MAILED: 12/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/649,944	ELLISON ET AL.	
	Examiner	Art Unit	
	JOHN PAK	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-20 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-20 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 12/03,5/04,10/04.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Claims 1-20 are pending in this application.

The following is a quotation of the first paragraph of 35 USC 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 18 is rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 18, which is directed to treating large cell lymphoma, was not disclosed in the originally filed disclosure. There is no mention of large cell lymphoma in the originally filed disclosure. At the time applicant's amendment (new claim 18) was filed, a preliminary amendment was not treated as part of the originally filed disclosure unless accompanied by a new oath or declaration that acknowledged the amendments. Such is not the case here; and consequently, treatment of a specific type of lymphoma that was not originally disclosed must be considered lacking in sufficient descriptive support from the originally filed disclosure, because applicant did not reasonably convey such treatment from the many different types of lymphomas.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in – (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United states before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for the purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-8 and 12 are rejected under 35 U.S.C. 102(e) as being anticipated by Zhang (US 6;720,011).

Zhang explicitly discloses treating lymphoma with arsenic trioxide. See column 1, lines 34-35 and 41-43. Intravenous composition containing 1-10 g arsenic trioxide, sodium chloride and water (column 1, lines 41-54). "[S]trong abruptive effect on the membranes of cancer cells" is disclosed, as well as inhibition of DNA/RNA synthesis (column 1, lines 58-61). Effective daily dose for an adult is disclosed as 10 ml of the composition containing 10 g/l arsenic trioxide added to 500 ml of 10% glucose solution is disclosed. This calculates to about 67 mg/day. Appropriate dose is to be "decreased accordingly for children" (column 2, lines 9-16).

Applicant's claims 1-8 and 12 are thereby anticipated. Ionic aqueous solution (applicant's claim 3) is met by the sodium chloride present in the arsenic trioxide solution (Zhang's column 1, lines 44-45). Varying the dose according to

the body weight of a human (applicant's claim 12) is met by Zhang's explicit disclosure to decrease the dose for children. The claims are thereby rejected.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 9-11 and 13-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang in view of CN 1121807 and Shimotsuura et al.

Zhang explicitly discloses treating lymphoma with arsenic trioxide. See column 1, lines 34-35 and 41-43. Intravenous composition containing 1-10 g arsenic trioxide, sodium chloride and water (column 1, lines 41-54). "[S]trong abruptive effect on the membranes of cancer cells" is disclosed, as well as inhibition of DNA/RNA synthesis (column 1, lines 58-61). Effective daily dose for an adult is disclosed as 10 ml of the composition containing 10 g/l arsenic trioxide added to 500 ml of 10% glucose solution is disclosed. This calculates to about 67 mg/day. Appropriate dose is to be "decreased accordingly for children" (column 2, lines 9-16).

CN 1121807 discloses administering arsenic trioxide as an injection to treat lymphatic cancer (page 4 of the English translation, last paragraph). The formulation of arsenic trioxide is referred to as "Ai Ling" (see pages 5-6 of the

English translation, in particular page 6, last full paragraph). Inhibition of DNA/RNA synthesis is disclosed (page 5 of the English translation, lines 6-7).

Shimotsuura et al. disclose that antineoplasmic actions of arsenic trioxide are primarily achieved by DNA composition blockage (page 25 of the English translation, top of page 49 in the original).

Zhang does not explicitly disclose treating lymphoma in a human by administering arsenic in combination with other chemotherapeutic or radiotherapeutic agents. Zhang also does not specify the lymphomas as Hodgkin's lymphoma, non-Hodgkin's lymphoma, follicular lymphoma, diffuse lymphoma, lymphoblastic lymphoma, large cell lymphoma, small lymphocytic lymphoma and HIV-related non-Hodgkin's lymphoma. However, for the reasons to follow, the claimed invention as a whole would nonetheless have been obvious to the ordinary skilled artisan in this field at the time the invention was made.

Zhang is clear in that arsenic trioxide is effective against "lymphoma." There is no limitation as to the type of lymphoma. Lymphoma is typically a Hodgkin's lymphoma or non-Hodgkin's lymphoma, so inclusion of both would have been obvious to the ordinary skilled artisan. Further, Zhang teaches a strong abruptive effect on the membranes of cancer cells and inhibition of DNA/RNA synthesis. Taken with teachings of Shimotsuura et al., which confirm the DNA composition blockage action of arsenic trioxide antineoplastic activity and teachings of CN 1121807, which expand on Zhang's teaching of efficacy against lymphoma by teaching efficacy against the broader "lymphatic cancer," the ordinary skilled artisan in this field would have been motivated to administer

arsenic trioxide to treat patients with the specific lymphomas recited in the instant claims. Additionally, since all of the lymphomas recited in applicant's claims are cancers of the lymphatic system with uncontrolled growth of cells of similar functions and origin, one having ordinary skill in the art would have been motivated to administer arsenic trioxide to treat such lymphomas, particularly in view of its adverse effect on rapid DNA replication.

As for combined use with radiation or other chemotherapeutic agents, such method would have been fairly suggested from the conventional practice in the cancer treatment field to combine the actions and benefits of several therapies to attack the cancer cells from a variety of mechanisms. The therapeutic agents listed in claim 11 are all well-known anti-cancer agents and inclusion of such additional anti-cancer agents in combination with arsenic trioxide would have been fairly suggested.

Therefore, the claimed invention, as a whole, would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention and the claimed invention as a whole have been fairly suggested by the teachings of the cited references.

Claims 9-11 and 13-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang in view of CN 1121807, Li et al. and Shimotsuura et al.

Zhang, CN 1121807 and Shimotsuura et al. are relied on for the same teachings as in the preceding ground of rejection. Discussion of their teachings there is incorporated herein by reference.

Li et al.[1] disclose treating 27 patients with malignant lymphoma, including Hodgkin's disease, with Ailin-1 (see the English translation on page 62). 70.37% remission rate reported (id.).

Li et al. add to the previous discussion of the prior art in that they provide clinical report of 70.37% remission after treating 27 patients with malignant lymphoma, including Hodgkin's disease. The transliteration of Li's chemo-therapeutic formulation is "Ailin-1." From CN 1121807, it is known that "Ai Ling" formulations contain arsenic trioxide. It is the Examiner's position that the ordinary skilled person in the art of treating lymphatic cancers (including those artisans in the U.S. and China) would have recognized various transliterations such as "Ailin-1" and "Ai Ling" to be the same or similar Chinese formulations, which all contain arsenic trioxide.

Hence, Li et al. add to the previously discussed body of knowledge concerning arsenic trioxide and lymphatic cancer efficacy by specifically teaching efficacy against Hodgkin's disease. In sum, Zhang teaches a strong abruptive effect on the membranes of cancer cells and inhibition of DNA/RNA synthesis. Taken with teachings of Shimotsuura et al., which confirm the DNA composition blockage action of arsenic trioxide antineoplastic activity and teachings of CN 1121807, which expand on Zhang's teaching of efficacy against lymphoma by teaching efficacy against the broader "lymphatic cancer," the ordinary skilled artisan in this field would have been motivated to administer arsenic trioxide to treat patients with the specific lymphomas recited in the instant claims,

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[1] Chinese J. Oncology, Vol. 10, pages 61-62 (1988).

particularly in view of Li et al. Additionally, since all of the lymphomas recited in applicant's claims are cancers of the lymphatic system with uncontrolled growth of cells of similar functions and origin, one having ordinary skill in the art would have been motivated to administer arsenic trioxide to treat such lymphomas, particularly in view of its adverse effect on rapid DNA replication.

As for combined use with radiation or other chemotherapeutic agents, such method would have been fairly suggested from the conventional practice in the cancer treatment field to combine the actions and benefits of several therapies to attack the cancer cells from a variety of mechanisms. The therapeutic agents listed in claim 11 are all well-known anti-cancer agents and inclusion of such additional anti-cancer agents in combination with arsenic trioxide would have been fairly suggested.

Therefore, the claimed invention, as a whole, would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention and the claimed invention as a whole have been fairly suggested by the teachings of the cited references.

For these reasons, all claims must be rejected.

Applicant is advised that several references listed on PTO-1449 were crossed out due to their (i) re-listing as the published documents, (ii) non-English language disclosure, or (iii) duplicate listings. Of the documents that are not

crossed out, several are not in the English language. The record should reflect the fact that such references are indicated as being considered (initialed) solely to the extent that the Examiner, who is not familiar with the French, German, Chinese and Japanese languages, could make out a cursory understanding of the disclosed topics therein. In this regard, applicant should note that only a search report from a **counterpart** foreign application can serve as a substitute for English language explanation of a document's relevance. To date, applicant has not clarified which of the many search reports cited in the PTO-1449 is for the counterpart foreign application to the instant application.

A facsimile center has been established in Technology Center 1600. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier number for accessing the facsimile machines is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Examiner John Pak whose telephone number is **(571)272-0620.** The Examiner can normally be reached on Monday through Friday from 8:00 AM to 4:30 PM. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's SPE, Mr. Gary Kunz, can be reached on **(571)272-0887**.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number **is (571) 272-1600**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have a question on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JOHN PAK
PRIMARY EXAMINER
GROUP 1600